Alice E. Till, Ph.D.
VICE PRESIDENT
SCIENCE POLICY AND TECHNICAL AFFAIRS

PhRMA

July 18, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 98D-0362; Draft Guidance for Industry on Stability Testing of Drug Substances and Drug Products; Notice of Availability and Request for Comments appearing in the *Federal Register* of June 8, 1998 (63 FR 31224)

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, happier and more productive lives. Investing more than $26 billion in 2000 in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

PhRMA submitted comments to the Docket on the referenced draft guidance on December 8, 1998 and additional comments on August 18, 2000. With this submission PhRMA wishes to further comment on the section in the draft stability testing guidance in which reference is made to a draft guidance entitled *Submission of Documentation in Drug Applications for Container Closure Systems used for the packaging of Human Drugs and Biologics* (June 1997) (lines 1127 – 1187).

Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics was finalized May 1999. Lines 1137 – 1187 of the draft stability guidance are, therefore, no longer necessary and PhRMA strongly recommends that they be deleted from the guidance. This recommendation is in keeping with prior suggestions from industry that FDA remove redundant information from the stability guidance and reference instead the appropriate final guidances (e.g., SUPAC and ICH).

Should FDA feel that they must retain the section PhRMA recommends be deleted, it is important to clarify that container orientation may be used to determine compatibility with a liquid drug product. As such, the impact of different orientations is usually considered as part of the package selection during development. Interaction effects can be assessed by performing stability studies with different container orientations during development. Other data on the composition and grade of contact material may also be used to support assessment of interaction effects.

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Once it has been justified in development that no interaction results from the contact between the container closure system and the product, it is not necessary to perform additional studies as long as the development studies are performed on the dosage form and the package that represent the final container closure system and product that is proposed for marketing.

If the assessment is not performed during development or the studies do not reflect the product and container closure proposed for marketing, the impact of orientation should be examined during formal stability studies.

Container closure orientation is not typically included as part of the post-approval commitments, but may need to be considered for impact of certain Post-Approval Package Changes.

PhRMA appreciates the opportunity to submit further commentary on the draft guidance. Please let us know if there are questions relating to the comments, or if the FDA needs additional information.

Sincerely,

Alice E Till

Alice E. Till, Ph.D.